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Brief Communication

Association of Novelty Seeking Scores and Striatal Dopamine D_2/D_3 Receptor Availability of Healthy Volunteers: Single Photon Emission Computed Tomography With ^{123}I-iodobenzamide

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It has been speculated that novelty seeking (NS) behavior is related to the dopaminergic system. Fifty-two subjects completed the Tridimensional Personality Questionnaire and underwent single photon emission computed tomography with ^{123}I-iodobenzamide. A marginally positive correlation was noted between NS and striatal dopamine D_2/D_3 receptor availability ($r=0.25$, $p=0.07$). A positive association was noted between the NS scores and left striatal D_2/D_3 receptor availability ($r=0.29$, $p=0.04$). The results suggest that a relationship might exist between NS score and dopaminergic activity.

Key Words: dopamine, iodobenzamide, novelty seeking, single photon emission computed tomography

Personality is a behavioral pattern that differs among individuals and is considered to be stable over time. Cloninger suggested that this behavioral property can be defined as the automatic associative response to emotional stimuli, and it might be heritable.[1] Several data collected from twin and family studies have proved this hypothesis, and Cloninger further elaborated his initial model to the four dimensions of temperament that are now well known.[1–4] The four temperament dimensions identified by Cloninger comprise novelty seeking (NS), harm avoidance (HA), reward dependence (RD) and persistence. Results on personality differences have been relatively consistent with the hypothesis of Cloninger. Meta-analysis have also largely supported Cloninger's theory of independent dimensions.[5]

Studies that have aimed to understand the correlation between personality traits and the

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neuroendocrine system have placed an emphasis on NS and the dopaminergic system.[2,3,6–9] Based on genetic studies, the NS trait is associated with the DRD4*7R allele at the D4 dopamine-receptor locus.[1–3,6,7,9,10] Dopamine agonist administration in young patients with Parkinson's disease has resulted in increased NS, which has highlighted the correlation between NS and the dopaminergic system.[11] However, there have only been a few imaging studies to date that have explored the relationship between NS and the central dopaminergic system.[7]

To measure directly the dopaminergic activity in the human brain is very difficult. Modern functional imaging methods, such as positron emission tomography and single photon emission computed tomography (SPECT) provide noninvasive, quantitative tools for direct measurement of dopamine function in the living human brain. Data from individuals with normal aging or Parkinson's disease have shown that increasing striatal D_2/D_3 availability ratio represents indirectly dopaminergic activity.[12]

The present study investigated directly the relationship between the NS personality trait and the central dopaminergic system in healthy volunteers.

Subjects and Methods

Subjects

We recruited 52 healthy volunteers (26 men and 26 women; mean age = 33.08 ± 11.28 years) from the community by advertisement. These participants were enrolled as controls in various studies. They were interviewed by a senior psychiatrist using the Chinese version of the Mini International Neuropsychiatric Interview[13] to exclude individuals with mental illnesses. None of the participants had a history of significant physical illness, illegal drug use, or cigarette use.

Before any procedure was performed, informed consent was obtained from the volunteers. The Ethics Committee for Human Research at the National Cheng Kung University Hospital approved the study protocols.

Measurements

SPECT acquisition and procedures

SPECT scanning with ^{123}I-iodobenzamide (IBZM) was used to measure striatal dopamine D_2/D_3 receptor binding. Before the SPECT examination, the thyroid gland was protected with 9 mL Lugol solution. Each subject was intravenously administered with 185 MBq (4.8 mCi) of ^{123}I-IBZM in a quiet environment about 10 minutes after inserting the intravenous lines. The radio equivalent dose was 0.042 mSv/MBq and is considered safe by Institute of Nuclear Energy Research of Taiwan. Imaging was initiated approximately 2 hours later by a triple-headed rotating gamma camera (Multispect 3; Siemens, IL, USA). The reconstructed transverse images were aligned parallel to the canthomeatal line.

The detailed imaging measurement was as described in our previous study.[14] The ratio of the radioactivity in the striatum and frontal cortex [(St–F)/F ratio] was derived by dividing the difference between the average counts per pixel in the striatum and the frontal cortex by the average counts per pixel in the frontal cortex. The ratio provided an objective estimation of striatal dopamine D_2/D_3 receptor availability, as determined in previous studies in which kinetic analyses were performed to explore the plateau of the time-activity curve.[15,16] A higher ratio indicated higher dopaminergic activity. All participants completed Tridimensional Personality Questionnaire (TPQ) and imaging procedures within 7 consecutive days.

Tridimensional Personality Questionnaire

The assessment of temperament traits was performed using Cloninger's TPQ, a 100-item questionnaire that measures three genetically distinct personality dimensions: NS, HA and RD; each of which consists of four lower-order dimensions.[17] The validity of the questionnaire seems to be high according to a large psychometric investigation in the general populations in Taiwan and Finland.[18,19] The NS subscales are exploratory excitability, impulsiveness, extravagance, and disorderliness.[18]

Statistical analysis

Pearson's correlation and partial correlation tests were conducted to explore the relationships between the NS scales and the striatal dopamine D_2/D_3 availability. The level of significance was set at $p < 0.05$ (two-tailed). All analyses were performed using SPSS version 10.0 (SPSS Inc., Chicago, IL, USA).

Results

After partialing out age, we found a marginally positive correlation between the NS scores and the striatal dopamine receptor availability ($r = 0.25$, $p = 0.07$) (Figure 1), and a significantly positive relationship with left (St-F)/F ratio of ^{123}I-IBZM ($r = 0.29$, $p = 0.04$) (Figure 2). However, no significant association was found between HA ($r = 0.13$, $p = 0.38$) or RD ($r = -0.02$, $p = 0.89$) scores and striatal dopamine D_2/D_3 availability (Table).

Discussion

The positive correlation between NS scores and striatal dopamine receptor availability was confirmed in our imaging study. Reduced NS scores in patients with Parkinson's disease have been reported, particularly with regard to dopamine receptor availability of the left side.[20] In our healthy volunteers, we also noted a correlation between NS scores and striatal dopamine D_2/D_3 receptor availability of the left side. The reason for the correlation with asymmetric dopamine deficiency is unknown.[20,21]

In addition, Zald et al reported a low number of available dopamine autoreceptors in subjects with high NS activity.[22] Zald et al proposed that the low number of receptors produces less autoinhibition of dopaminergic cell firing and consequently leads to more dopamine release. Our study focused on the dopamine receptor availability and confirmed the relationship between NS score and dopaminergic activity.

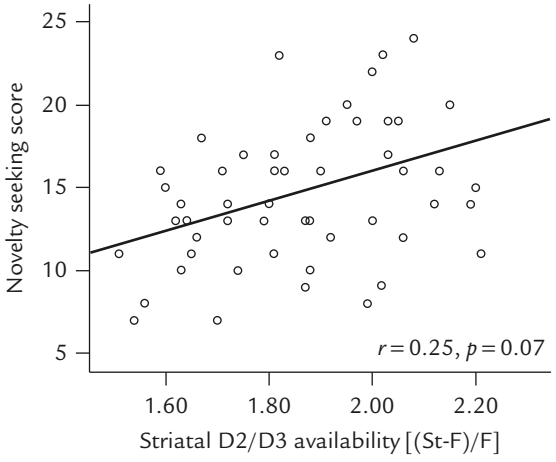

Figure 1. The correlation between NS scores with striatal D_2/D_3 availability.

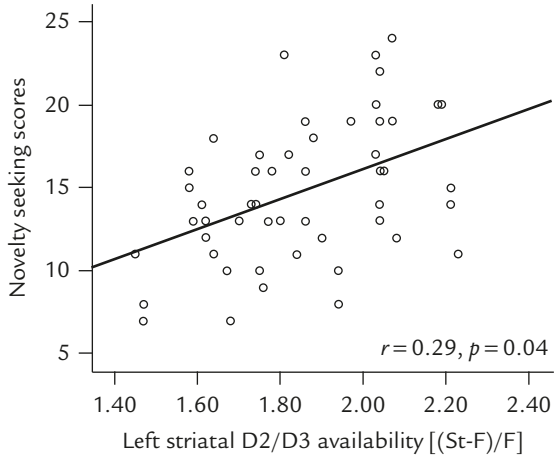

Figure 2. The correlation between NS scores with left striatal D_2/D_3 availability.

Table. Correlations between Tridimensional Personality Questionnaire scores and striatal D_2/D_3 ratio ($n = 52$)

	Novelty seeking		Harm avoidance		Reward dependence	
	r	*p*	*r*	*p*	*r*	*p*
(St-F)/F ratio	0.25	0.07	0.13	0.38	–0.02	0.89
Left (St-F)/F ratio	0.29	0.04	0.09	0.52	–0.02	0.90
Right (St-F)/F ratio	0.01	0.93	0.16	0.25	–0.02	0.90

Our results should be interpreted with caution due to the following limitations. First, the subjects might not be representative of the general population because of the limited sample size and being middle aged. Second, the imaging technique focusing on striatum was not able to detect all the other central dopamine tracts. Third, we did not explore the binding affinity of different receptor polymorphisms. Fourth, no toxicological screening was done. Finally, this was an association study. It did not rely upon experimental manipulation of the dopaminergic tone to induce changes in NS scores, therefore, the causal relationship between striatal dopaminergic activity and NS scores cannot be confirmed.

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